



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460

MAR 16 1992

OFFICE OF  
PESTICIDES AND TOXIC SUBSTANCES

Memorandum:

SUBJECT: FAP#6H5487. Diflubenzuron Metabolism in the Goat. Dated May 11, 1989. Submitted October 17, 1991. (DEB# 8957, MRID #'s 420609-00 and -01).

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THRU: Philip V. Errico, Section Head  
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and

Toxicology Branch  
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Duphar Chemical Company of Graveland, Holland has submitted cover letter dated October 17, 1991 and a metabolism study dated May 11, 1989, entitled "The Disposition of 14C-Diflubenzuron in the Lactating Goat", (Duphar Report #56645/02/1990).

Conclusions/Recommendations:

The submitted goat metabolism study is incomplete. The data gap stated in the Reregistration Standard update dated 6/21/91 is not resolved. Identification of residues is needed.

Detailed Considerations:

CBTS had previously reviewed a proposed protocol entitled "The Disposition of 14C-Diflubenzuron in the Lactating Goat (IRI Project #138261, Duphar #C.303.63.002) (See memo of 10/6/88, S. Malak). At

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that time, CBTS recommended changes/additions to the proposed study. A minimum dosage of 14 ppm was recommended in order to obtain sufficient residues in milk and tissues. CBTS also recommended that the protocol include isolation, identification, and quantification of diflubenzuron, and any metabolites containing the p-chlorophenylamine moiety, including p-chloroaniline, a complete description of the methodology employed for the above residues, and confirmation of structures with mass spectrometry. The cut-off level for identification of residues was suggested at 20 ppb.

The submitted study (Duphar#56645/02/1990) dosed orally twice daily for 3 days four goats with either 0.1 (1 and 3) or 2.5 (4 and 5) mg/kg body weight <sup>14</sup>C-diflubenzuron uniformly labelled in both phenyl rings. The levels of total radioactivity in tissues, organs, and milk are expressed as ug/g equivalents (ppm) in the following table.

<u>Sample</u>	<u>Animal Number</u>			
	<u>1</u>	<u>3</u>	<u>4</u>	<u>5</u>
Muscle	0	0.001	0.02	0.05
Fat	0.003	0.004	0.12	0.30
Liver	0.22	0.26	3.2	6.1
Kidney	0.019	0.016	0.36	1.0
Milk (max. value)	0.009	0.007	0.22	0.22

The above values show that diflubenzuron residues (parent and/or metabolites) are present in levels that would yield to isolation and identification of residues in all organs, tissues, and milk, especially with the higher dosage of 2.5 mg/kg body weight. The registrant did not attempt isolation or identification of the residues.

Therefore, CBTS will require the registrant to isolate and identify the residues in the goat organs, tissues, and milk. Also, in future metabolism studies submitted for Agency review, levels of diflubenzuron should be reported as ppm in the feed. If residues are identified, then additional feeding studies may be required.

The data gap stated in the Reregistration Standard update dated 6/21/91 is not resolved. Identification of residues is needed.

#### Other Considerations:

In a previous metabolism study, for extraction of the residues, milk was partitioned with ethyl acetate and dilute aqueous acid

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(pH 2). The organic layer was evaluated by thin-layer chromatography, but the aqueous was not investigated further. Based upon the alkaline characteristic of 4-chloroaniline, it could partition into the initial dilute acid wash. CBTS does not have data to support the notion that any 4-chloroaniline residue would be remain in the acidic layer in the initial partition with ethyl acetate and dilute acid (pH 2). This information would be advantageous for the risk assessment for dimilin. The registrant could design an experiment with <sup>14</sup>C-4-chloroaniline to provide this data.

cc: FAP#6H5487; J. Stokes (CBTS); E. Zager (CBRS); C. Furlow (PIB/FOD); diflubenzuron S.F.; R.F.; Circulation (7)  
RDI: Perrico:3/4/91:RLoranger:3/5/91  
H7509C:CBTS:JStokes:js:Rm 803A:CM#2:305-6439:3/6/91

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